

REMARKS

This responds to the Office Action mailed on July 18, 2008.

Claims 133, 170, 174, and 178 are amended, no claims are canceled, and no claims are added; as a result, claims 132-134, 137-139, and 168-220 are now pending in this application. Support for the amendments to claims 133, 170, 174, and 178 can be found at least at page 34, lines 29-33 and at page 59, lines 16-25. Accordingly, no new matter has been added by way of any amendment.

§112 Rejection of the Claims, First Paragraph

Claims 132-134, 137-139, and 168 were rejected under 35 USC § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is respectfully traversed.

At page 2 of the Office Action, last paragraph, the Examiner acknowledges that the specification enables the claims with respect to luciferin derivatives. Applicants thanks the Examiner for this favorable assessment. However, the Examiner appears to reject claims 132-134, 137-139, and 168 merely because of the recitation of the term "compound", stating that the claims are not enabled for all compounds without limitation. Applicants' claims are not directed to all compounds without limitation. M.P.E.P. 2164.06 states that "The examiner should determine what each claim recites and what the subject matter is when the claim is considered as a whole, not when its parts are analyzed individually."

Claims 132-134, 137-139, and 168 are not directed to "all compounds". Claims 132-134 and 168 are directed to a specific group of compounds and compositions. The metes and bounds of the group of chemical compounds are clearly defined by the structural definition recited in claim 132, as well as the functional limitation recited in claim 132 ("[a] compound that is a substrate of a cytochrome P450 enzyme and a pro-substrate of a luciferase enzyme"). One skilled in the art would readily understand the scope of the compounds claimed by Applicants. Accordingly, Applicants respectfully requests that the Examiner examine each claim as a whole and give appropriate weight to the elements recited in each claim. When each claim is read as a

whole, the specification enables one skilled in the art to make and use the invention commensurate in scope with the claims.

Applicants note that claims 137-139 are directed to certain specific chemical compounds, which are specifically named in the claims. The names of these compounds are fully supported by the specification and are illustrated in Figure 2. The preparation of each of the recited compounds is described in the specification in Example 1 at pages 52-59. Methods of using the compounds are described throughout the specification. Working examples of the use of these and other compounds are described in Examples 2-16 at pages 59-73. Therefore the specification enables one skilled in the art to make and use the invention commensurate in scope with the claims.

Applicants further note the statement in the Office Action, fourth line from the end of page 3: "The nature of the invention is a process of making a metal complex." Applicants believe this statement is an editorial error. The nature of the invention is luminescence-based methods and probes for cytochrome p450 activity.

Also, the last paragraph of page 3 states that the "breadth of the claims encompass all compounds, wherein there is no structural limitation other than it is a substrate of a cytochrome P450 enzyme and a pro-substrate of a luciferase enzyme." (Emphasis added.) This statement is incorrect. Claim 132 (and its dependent claims) recites that the compound "is a structural analog of luciferin, dehydroluciferin or luciferol that includes a substitution at the 6' hydroxy site of luciferin or luciferol or the corresponding 6' site of dehydroluciferin, which substitution includes C₁₋₂₀ alkoxy or C₁₋₂₀ alkenyloxy wherein the alkoxy and alkenyloxy are substituted with halogen, hydroxy, amino, cyano, azido, heteroaryl or aryl substituted with haloalkyl; or C₃₋₂₀ alkynyloxy; cycloalkoxy, cycloalkylamino, C₁₋₂₀ alkylamino, diC₁₋₂₀ alkylamino, C₂₋₂₀ alkenylamino, diC₂₋₂₀ alkenylamino, C₂₋₂₀ alkenyl C₁₋₂₀alkylamino, C₃₋₂₀ alkynylamino, diC₃₋₂₀ alkynylamino, C₃₋₂₀ alkynyl C₁₋₂₀alkylamino, or C₃₋₂₀ alkynyl C₂₋₂₀alkenylamino, wherein each of the above groups are optionally substituted with halogen, hydroxy, amino, cyano, azido, heteroaryl or aryl substituted with haloalkyl." All of the preceding language constitutes structural description that defines the metes and bounds of the claim. The specification describes the subject matter of the claims such that one skilled in the art can make and use the invention commensurate in scope with the claims.

Page 4 of the Office Action discusses that the compounds and compositions as currently claimed would read on a large number of compounds and compositions, and that "it would cause a skilled artisan an undue amount of experimentation to determine which products are being claimed." When analyzing whether "undue experimentation" is required to practice a claimed invention, the key word is "undue" not "experimentation." *In re Angstadt*, 190 U.S.P.Q. 214, 219 (C.C.P.A. 1976). Enablement is not precluded by the necessity for some experimentation, such as performing routine assays or synthetic reactions. In fact, a considerable amount of experimentation is permissible if the experimentation is merely routine, or if the specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should take. *Ex parte Jackson*, 217 U.S.P.Q. 804, 807 (Bd. App. 1982). At the last paragraph of page 4, the Office Action indicates that there is an absence of direction or guidance (or working examples) in the specification". Applicant respectfully disagrees with the Examiner's assertion. The Examiner's attention is directed to Example 1, which provides seven pages of guidance to the skilled artisan for preparing compounds of claim 132 (and specifically, the compounds of claims 137-139). Other compounds within the scope of claim 132 can be readily prepared by one skilled in the art by using alternative starting materials for the reactions described on pages 52-59. The specification at page 75, lines 9-17, also makes reference to useful procedures known in the art for preparing useful starting materials for various compounds. As discussed above, working examples of the use of these and other compounds are described in Examples 2-16 at pages 59-73. Thus the specification does provide working examples and guidance to one of skill in the art to make and use Applicants' claimed compounds.

Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 132-134, 137-139, and 168.

§112 Rejection of the Claims, Second Paragraph

Claims 132, 137-139, 169, 173 and 177 were rejected under 35 USC § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. This rejection is respectfully traversed.

On page 5 of the Office Action, claims 132, 137-139, 169, 173 and 177 were rejected because they include the terms luciferin, luciferol, and/or dehydroluciferin. The Examiner

asserts that the terms luciferin, luciferol, and dehydroluciferin are trademarks or trade names, and cited Ex Parte Simpson in support of the rejection. Applicants respectfully points out that the terms luciferin, luciferol, and dehydroluciferin are not trademarks. Therefore, Ex Parte Simpson does not support the rejection and is not applicable to Applicants' claim terms.

The terms luciferin, luciferol, and dehydroluciferin can be, however, used to identify the respective compounds. M.P.E.P. 608.01(v) states that "[n]ames used in trade are permissible in patent applications if: (A) Their meanings are established by an accompanying definition which is sufficiently precise and definite to be made a part of a claim, or (B) In this country, their meanings are well-known and satisfactorily defined in the literature."

Applicant respectfully notes that both conditions (A) and (B) are met in the instant case. For example, each of luciferin, luciferol, and dehydroluciferin are illustrated in Figure 2, so the terms are therefore accompanied by definitions that are sufficiently precise and definite. Also, the terms are also well-known in the literature. For the term "luciferin", see WO 2001/020002 (of record), cited at page 75, line 4, of the instant application. For the term "luciferol", see U.S. Patent No. 4,857,457 at column 2, line 64 and U.S. Patent No. 6,228,392 at column 11, line 52 (copies enclosed). For "dehydroluciferin", see Fontes et al., Biochemical and Biophysical Research Communications, Volume 237, Issue 2, 18 August 1997, Pages 445-450, titled "Synthesis of Dehydroluciferin by Firefly Luciferase: Effect of Dehydroluciferin, Coenzyme A and Nucleoside Triphosphates on the Luminescent Reaction" (copy of abstract enclosed).

Therefore luciferin, luciferol, and dehydroluciferin are terms whose meanings are established by definitions in the specification, as well as terms that are well-known in the literature. Accordingly, reconsideration and withdrawal of the rejection of claims 132, 137-139, 169, 173 and 177 is respectfully requested.

§112 Rejection of the Claims, Second Paragraph

Claims 132-134, 137-139, 168, 169, 171-173, 175-177 and 179-180 were rejected under 35 USC § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. This rejection is respectfully traversed.

The Office Action applies this rejection to the terms luciferin, luciferol, dehydroluciferin, and pyrophosphatase. The Examiner asserts that the metes and bounds of the terms are broader than the disclosure. Applicants respectfully disagree with the Examiner's assertion for the reasons discussed in the rejection immediately above. Their metes and bounds are well established and well-known to those of skill in the art. Furthermore, the term "pyrophosphatase" is also well understood in the art and is defined in the specification at page 31, line 1 to page 32, line 8.

At the top of page 6, the Examiner states that "that incorporation into claims by express reference to the specification is not permitted", citing Ex parte Fressola in support of the assertion. However, Ex parte Fressola concerns a so called "omnibus" claim. Claims 132-134, 137-139, 168, 169, 171-173, 175-177 and 179-180 are not omnibus claims and do not expressly reference the specification. Accordingly, Ex parte Fressola does not support the rejection and is not applicable to Applicants' claims. The terms luciferin, luciferol, dehydroluciferin, and pyrophosphatase are readily understood by those of skill in the art, and their meanings are clearly defined by the specification, as noted above. The claims do not include express reference to the specification, as suggested by the Examiner. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

§112 Rejection of the Claims, Second Paragraph

Claims 132-134, 137-139 and 168-180 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly failing to comply with the written description and enablement requirement. This rejection is respectfully traversed.

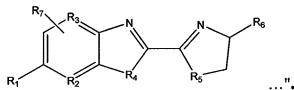
At page 6 of the Office Action, the Examiner asserts that the definitions of the terms R₁, R₂, R₃, R₄, and R₅ are not supported by the specification, claims or drawings. The Examiner invited Applicants to point out where in the original specification, claims or drawings the terms are supported and defined. Applicants direct the Examiner's attention to the specification at page 17, line 30 to page 18, line 25, as well as original claim 135 at page 95, line 15, where the terms R₁, R₂, R₃, R₄, and R₅ are recited and defined. The values within the definitions of each of R₁, R₂, R₃, R₄, and R₅ are commonly used chemical groups or elements that are clear to those of skill

in the art. Applicants invite the Examiner to point out any term within the definitions of R₁, R₂, R₃, R₄, and R₅ that would be unclear to one of skill in the art.

At page 6, the Examiner also stated that "[t]he instantly claimed invention is D-luciferin, which is defined in Figure 2". (Emphasis added.) This is an incorrect statement. The instantly claimed invention is defined by the pending claims, none of which encompass the compound D-luciferin itself. The pending claims are directed to compounds that are "structural analogs of luciferin, dehydroluciferin or luciferol" (claim 132), specific luciferin derivatives (claims 137-137) and compounds of the formula shown in claim 169, which are also derivatives of luciferin. Claims 190-220 are further directed to kits that include structural analogs of luciferin, dehydroluciferin or luciferol, and other specific compounds (see claims 190 and 211, respectively).

The Examiner further stated that "D-luciferin's core compound always contains an oxygen at the R₁ position, carbon at the R₂ and R₃ positions, and sulfur at the R₄ and R₅ positions. No other atom or functional group at those positions are supported by the instant specification, drawings, or claims." These are incorrect statements. Figure 2 illustrates D-luciferin itself, and 13 derivatives of D-luciferin. Dehydroluciferin is an example of a luciferin derivative in Figure 2. Dehydroluciferin does not include an oxygen atom at the 6'-position of the luciferin core structure. Thus, derivatives of D-luciferin are not limited to the narrow interpretation set forth by the Examiner.

Applicant also notes that the formula found at the top of page 18 shows R₁ at the 6'-position of the luciferin core structure. The variable R₁ is defined as several different groups such that the R₁ position is not required to be oxygen, but can be any of the groups listed at page 18, lines 4-12. At page 17, bridging to page 18, the specification states that "a D-luciferin derivative of the invention is provided having the formula:



The formula clearly shows that "a D-luciferin derivative of the invention" includes D-luciferin derivatives that have substitutions at R₁ other than oxygen, as well as various substitutions at R₂, R₃, R₄, and R₅. Thus, the luciferin derivatives claimed by Applicant do not require an oxygen at

the R₁ position, carbon at the R₂ and R₃ positions, and sulfur at the R₄ and R₅ positions, as suggested by the Examiner. Therefore, the claims are supported by the specification and the original claims. Reconsideration and withdrawal of the rejection is respectfully requested.

§112 Rejection of the Claims, Second Paragraph

Claims 132-134, 137-139, 168-180 were rejected under 35 USC § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. This rejection is respectfully traversed.

The Examiner specifically pointed to the definition of R₁ in claim 135. Applicants respectfully point out that claim 135 has been cancelled. The Examiner's comments will be addressed as if they were intended to be applied to pending claim 169, which includes a corresponding term "R₁".

The Examiner stated that the definition of R₁ is indefinite because the claim is directed to D-luciferin derivatives. It is respectfully submitted that claim 169 does not recite "D-luciferin derivatives". Claim 169 claims compounds of the recited formula, where the definition of R₁ is clearly defined as would be readily understood by one skilled in the art.

The Examiner further states that "[a]ll of the D-luciferin derivatives of Figure 2 and the specification contain an oxygen atom at the 6'-position. Therefore, the definition of R₁ must contain oxygen and cannot be substituents such as hydrogen alone." Applicants strongly reject these statements. Not all of the D-luciferin derivatives in Figure 2 contain an oxygen atom at the 6'-position. The Examiner's attention is directed to the structure of dehydroluciferin in Figure 2, which has a hydrogen at the 6'-position. Additionally, the D-luciferin derivatives in the specification at page 17, line 30, to page 18, line 25, show a variety of D-luciferin derivatives that do not require an oxygen atom at the 6'-position of the derivative. Therefore, it is respectfully submitted that the definition of "R₁" is definite and clear to one of skill in the art, and supported by Applicants' specification. Reconsideration and withdrawal of the rejection is respectfully requested.

Applicants further note that claims 132-134, 137-139, and 168 do not include a term "R₁". Clarification from the Examiner is respectfully requested with respect to how this rejection could apply to those claims.

Double Patenting Rejection

Claims 132-142 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-24, 68-71, and 91 of copending U.S. Patent Application Serial No. 11/444,145.

Applicants note that claims 135-136 and 140-142 have been cancelled, therefore the rejection does not apply to those claims. Applicants further note the Examiner's statement in the first paragraph found at page 11 of the Office Action, which states "In the instant application R1 can only be oxygen substituted moieties." This is an incorrect statement because the definition of Applicants' R₁ (see for example, claim 169) can be other than oxygen substituted moieties.

The Examiner stated that the provisional rejection will be withdrawn should all other issues be resolved. Applicants respectfully submit that the claims are in condition for allowance and withdrawal of the provisional rejection is respectfully requested.

Objections to the Claims

Claims 133, 170, 174, and 178 were objected to under 37 C.F.R. 1.75 as allegedly being substantial duplicates of claims from which they depend. The Examiner pointed to claims 132, 169, 173, and 177 in support of the rejection, and noted that composition claims 133, 170, 174, and 178 include only one element. The Examiner further noted that composition claims should include a minimum of two elements. Claims 133, 170, 174, and 178 have been amended to recite the additional term "buffer". Support for the amendments can be found at least at page 34, lines 29-33 and at page 59, lines 16-25. The amendments are believed to obviate the objection to claims 133, 170, 174, and 178. Reconsideration and withdrawal of the objection is respectfully requested.

Allowable Subject Matter

Claims 181-189 were objected to as being dependent upon a rejected base claim, but were indicated to be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Applicants thank the Examiner for this favorable

assessment. Each of the pending claims are now believed to be in condition for allowance and notification to that effect is earnestly requested.

Request for Rejoinder

In responses filed July 24, 2006 and June 19, 2008, Applicants requested rejoinder of the withdrawn claims upon a notice of allowable subject matter for the claims under examination. Applicant believes that claims 132-134, 137-139, and 168-189 are now in condition for allowance. Accordingly, the Examiner is respectfully requested to rejoin the subject matter of original claims 116-126 and 130-131 ("kit" claims), which now correspond to claims 190-220. The subject matter of original claims 116-126 and 130-131 that is directed to compounds has been amended in a manner corresponding to the amendments to the elected compound claims (see, e.g., compound claim 132 and kit claim 190, and compound claim 169 and kit claim 199). Examination and allowance of claims 190-220 is respectfully requested.

CONCLUSION


Applicant respectfully submits that the claims are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney ((612) 359-3270) to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

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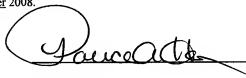
Date 10/20/2008

By 
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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being filed using the USPTO's electronic filing system EFS-Web, and is addressed to: MS Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on this 20th day of October 2008.

Patricia A. Hultman

Name



Signature